STIC search results 7/12/05

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doi:10.1016/S1071-5576(00)00106-4 Cite or Link Using DOI

Oxidative stress and the ovary*1

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Available online 19 February 2001.

Abstract

Superoxide (O_2^-), hydrogen peroxide (H_2O_2), and lipid peroxides are generated in luteal tissue during natural and prostaglandin-induced regression in the rat, and this response is associated with reversible depletion of ascorbic acid. Reactive **oxygen** species immediately uncouple the luteinizing hormone receptor from adenylate cyclase and inhibit steroidogenesis by interrupting transmitochondrial cholesterol transport. The cellular origin of **oxygen** radicals in regressing corpora lutea is predominately from resident and infiltrated leukocytes, notably neutrophils. Reactive **oxygen** species are also produced within the follicle at ovulation and, like the corpus luteum, leukocytes are the major source of these products. Antioxidants block the resumption of **meiosis,** whereas the generation of reactive **oxygen** induces oocyte maturation in the follicle. Although **oxygen** radicals may serve important physiologic roles within the ovary, the cyclic production of these damaging agents over years may lead to an increased cumulative risk of ovarian pathology that would probably be exacerbated under conditions of reduced antioxidant status.

Author Keywords: **Oxygen** radicals; antioxidants; corpus luteum; follicle; oocyte

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Dependence of mitosis and respiration in roots upon oxygen tension

By J. E. Amoore

Department of Botany, University of Edinburgh

(*Communicated by R. Brown, F.R.S.—Received* 12 *July* 1960—*Read* 16 *February* 1961)

Excised pea-root tips were incubated for 4 h in gas mixtures containing 0·00001 to 100% oxygen, in order to determine the effect upon mitosis. Below 0·0005% oxygen, mitosis was completely arrested. Between 0·001 and 0·02% oxygen, cells initially in mitosis completed division, but no more cells started dividing. Between 0·05 and 0·2% oxygen, cells initially in interphase entered division, but did not finish. Above 0·5% oxygen, all cells not prevented from dividing by excision finished division within 4 h. After exposure to 0·05% oxygen for 4 h, an excessive proportion of cells was found in prophase; in 0·1% oxygen an excess of metaphases, and in 0·2% oxygen an excess of telophases resulted.

The oxygen uptake and carbon dioxide output of root tips were measured in a range of oxygen tensions and in anaerobic conditions. The relationship between oxygen uptake and oxygen tension was hyperbolic; a half maximum rate of oxygen uptake was obtained at about 10% oxygen. It was concluded that the respiration of root tips was limited by slow diffusion of oxygen through the tissue. From the carbon dioxide output it was estimated that the amount of energy available to isolated root tips under anaerobic conditions was about 1% of that available under aerobic conditions.

Possible mechanisms whereby extreme oxygen-lack could arrest mitosis were considered. It was shown that the arrest was not due to abolition of a gross supply of energy. No evidence was obtained as to what other mechanism might be operative. An hypothesis was formulated in an attempt to explain the complicated relationship between mitosis and oxygen tension. It was assumed that the visible phases of mitosis are immediately preceded by a phase with a higher requirement for oxygen than mitosis, and that preceding this is an earlier phase with a lower oxygen requirement than mitosis.

Introduction

In the preceding paper (Amoore 1961) it was shown that acute oxygen-lack c cyanide poisoning could arrest mitoses occurring in pea-root tips. However, the conditions were not thoroughly anaerobic, mitoses in progress were able t continue slowly. The experiments described below were designed to investigat in detail the relationships between oxygen-tension, mitosis and respiration i excised pea-root tips.

Methods

General methods

The general experimental methods were as previously described (Amoore 1961 Excised root tips from 48 h pea seedlings (*Pisum sativum* var. Meteor) wer used throughout. In one experiment (see table 5) fifty-five root tips held in perforated plate were cut simultaneously with a razor as described by Brown Rickless (1949). For determining the mitotic index, use was frequently made c

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Dependence of Mitosis and Respiration in Roots upon Oxygen Tension, by J. E. Amoore
Proceedings of the Royal Society of London. Series B, Biological Sciences © 1961 The Royal Society

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Theriogenology
Volume 49, Issue 2 , 15 January 1998, Pages 483-497

doi:10.1016/S0093-691X(97)00420-2 Cite or Link Using DOI

Controlling meiotic resumption in bovine oocytes: A review

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Received 19 September 1997; accepted 20 November 1997. ; Available online 30 March 1998.

Abstract

Meiotic arrest refers to the nuclear stage of the oocytes within the follicles. Meiotic resumption occurs when oocytes are isolated from their follicular environment and placed in a simple maturation medium. The sine qua none condition for meiotic resumption is that the oocytes must be competent to resume meiosis. It has been shown that competent oocytes must reach a minimum diameter before been able to resume meiosis. In the bovine, competent oocytes measure at least 110 μm in diameter (24, 39).

It appears that the inhibitory factors of meiotic resumption might only be necessary after the oocyte has acquired its competence. However, once the oocytes become competent, they need these factors to maintain meiotic arrest. It is generally recognized that follicular cells produce inhibitors necessary to maintain the oocyte in meiotic arrest. The removal of the oocyte from its follicular environment deprives the oocyte of inhibitory factors. Oocytes then resume meiosis (63). This article will first review the different chemical modulators to emphasize the importance of protein synthesis and the role of different kinases and phosphatases. Then it will review the follicular aspects involved in the control of meiotic arrest of oocytes competent to resume meiosis.

Author Keywords: BFF; inhibitor; maturation; meiosis; oocyte

Corresponding author. Correspondence and reprint requests. Fax: 418-656-3766.

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File 350:Derwent WPIX 1963-2005/UD,UM &UP=200543
         (c) 2005  Thomson Derwent
File 347:JAPIO Nov 1976-2005/Feb(Updated 050606)
         (c) 2005 JPO & JAPIO
Set     Items   Description
S1         13   MEIOSIS()(ACTIVAT? OR INDUC???)()(SUBSTANCE? ? OR STEROL? ?)
S2     329736   OXYGEN OR O2
S3     413923   VACUO OR VACUUM
S4      33540   FREEZE()(DRY??? OR DRIES OR DRIED)
S5        813   (MOLE OR MOLES)(1W)(LITER OR LITRE)
S6    4356833   LOW OR LOWER OR REDUCED OR ABSENCE OR MINOR
S7    1761746   CONTAINER? ? OR CHAMBER? ? OR RECEPTACLE? ? OR CANISTER? ?
             OR VESSEL? ? OR VIAL? ? OR CAPOUL? ? OR DISH OR DISHES
S8    1063437   SEAL?? OR SEALING OR ENCLOS????
S9    1184507   CLOSE OR CLOSES OR CLOSED OR CLOSING OR AIRTIGHT OR AIR()T-
            IGHT OR HERMETIC?
S10   1997976   STORE? ? OR STORING OR STORAGE OR PRESERV?
S11       613   VITRO()(FERTILI?ATION OR MATURATION) OR IVF OR IVM
S12    331214   IC=(A61K-031? OR B65D-083? OR B65D-085?)
S13     23638   IC=(A61J-001? OR A61J-003? OR C12M-003?)
S14         1   S1 AND S2:S4 [a duplicate]
S15       190   MEIOSIS
S16       103   MEIOTIC
S17       254   S15:S16
S18        13   S2:S4 AND S17
S19        12   S18 NOT S14
S20         2   S19 AND S7:S11
S21        10   S19 NOT S20
S22    459567   S6(3N)S2 OR S3:S4
S23     27174   S10 AND S22
S24    131620   S7(2N)S8:S9
S25      1537   S23 AND S24
S26         0   S11 AND S25
S27        94   S12 AND S25
S28        42   S13 AND S25
S29       125   S27:S28
S30     18423   MEIOTIC OR STEROL? ?
S31         0   S29 AND S30
S32        23   S24/TI AND S29
S33        12   S1 NOT (S14 OR S20 OR S21 OR S32)
S34      1166   OOCYTE? ?
S35        40   S22 AND S34
S36         4   S24 AND S35
S37        15   S35 AND S10
S38         1   S36 AND S37
S39        16   S36:S37 NOT (S14 OR S20 OR S21 OR S1 OR S32 OR S38)
S40       233   S22 AND S24 AND S12
S41         1   S11 AND S40 [a duplicate]
S42         3   S40 AND (S15 OR S30)
S43         2   S42 NOT (S14 OR S20 OR S21 OR S1 OR S32 OR S38 OR S39 OR S41)

20/26,TI/2     (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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014707166
WPI Acc No: 2002-527870/200256
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Cloning animal with cell at G1-phase of cell cycle comprises culturing animal cells to confluence, introducing cells/genome of cells into enucleated oocyte to obtain reconstructed embryos and developing embryo to obtain animal

20/34/1 (Item 1 from file: 350)

DIALOG(R)File 350:Derwent WPIX

015924350
WPI Acc No: 2004-082190/200408

System useful for in vitro producing mammalian pre-embryo, comprising units for obtaining mammalian oocyte, mammalian spermatozoa, apparatus comprising entrance port, exit port and communication port

Patent Assignee: KOBENHAVNS AMTS SYGEHUS H (KOBE-N); KOBENHAVNS AMTS SYGEHUS H (SYGE-I)
Inventor: LINDENBERG S
Number of Countries: 105 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 2003106662	A1	20031224	WO 2003DK401	A	20030617	200408 B
AU 2003232183	A1	20031231	AU 2003232183	A	20030617	200451
EP 1539932	A1	20050615	EP 2003759883	A	20030617	200540
			WO 2003DK401	A	20030617	

Priority Applications (No Type Date): US 2002407686 P 20020904; DK 2002924 A 20020617; DK 2002925 A 20020617; US 2002407685 P 20020904
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 2003106662	A1	E	99	C12N-005/06	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

AU 2003232183	A1		C12N-005/06	Based on patent WO 2003106662
EP 1539932	A1	E	C12N-005/06	Based on patent WO 2003106662

Designated States (Regional): AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

Abstract (Basic): WO 2003106662 A1

NOVELTY - System (I) for in vitro producing mammalian pre-embryo, comprising unit (II) for obtaining mammalian oocyte (III), unit (IV) for obtaining mammalian spermatozoa (V), apparatus (VI) having separate **air - tight chambers** , where (VI) comprises entrance port communicating with (II) and/or (IV), exit port for withdrawal of pre-embryo, communication port allowing transfer of (III), (V) and/or pre-embryo between **chambers** , is new.

DETAILED DESCRIPTION - System (I) for in vitro producing a mammalian pre-embryo, comprising:

(a) unit (II) for obtaining a mammalian oocyte (III);

(b) unit (IV) for obtaining a mammalian spermatozoa (V);

(c) an apparatus (VI) having two or more separate **air - tight chambers** , for which the **oxygen** tension of one **chamber** is changed independent of the **oxygen** tension of the other **chamber** , where the **chambers** constitute a main **chamber** and a residence **chamber** , (VI)

comprises an entrance port capable of communicating with (II) and/or (IV);

(d) an exit port for withdrawal of the pre-embryo, and

(e) a communication port between the two **chambers** allowing transfer of (III), (V) and/or pre-embryo between the **chambers** .

INDEPENDENT CLAIMS are also included for the following:

(1) in vitro producing (M1) a mammalian pre-embryo, comprising:

(a) providing (III) and (V);

(b) culturing (III) and (V);

(c) fertilizing (III) with (V) to obtain a fertilized (III); and

(d) allowing cell-division for the fertilized (III) to obtain a multicellular pre-embryo, where providing or culturing step is conducted at an **oxygen** tension below 15 %;

(2) in vitro producing (M1) a mammalian pre-embryo, comprising:

(a) providing gametes chosen from (III) and (V); and

(b) carrying out the method of (1), where the culture is performed at an **oxygen** tension allowing cultivation of the cells and one of the steps comprises a change in the **oxygen** tension;

(3) implanting (M2) a pre-embryo, comprising culturing (III) and (V), and transferring the resulting pre-embryo to the uterus of a mammalian female;

(4) producing (M3) a stem cell (VII), comprising:

(a) providing a multicellular embryo obtained by (M1);

(b) isolating the multicellular pre-embryo;

(c) isolating cells from the inner cell mass of the pre-embryo;

(d) culturing the isolated cells from the inner cell mass in a matrix gel; and

(e) obtaining (VII);

(5) (VII) obtained by (M3);

(6) a stem cell line obtained from (VII); and

(7) stem cell package comprising (VII), certificate describing the culture conditions for (VII) and the cell cultures from which (VII) is obtained.

USE - (I) is useful for culturing cell cultures, gametes, embryos, blastocysts, stem cells and stem cell lines. (VII) is useful for producing stem cell line (claimed).

ADVANTAGE - (I) enables production of mammalian pre-embryo and stem cells with better quality.

pp; 99 DwgNo 0/3

Technology Focus:

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred System: In (I), (II) is a system with a needle communicating under **air - tight** conditions with a unit for transferring from needle to (VI), where the unit for transferring comprises syringe and tube. (IV) is a system in which the **oxygen** tension is controlled. The atmosphere within the **chambers** is kept aseptic. The temperature of each **chamber** is regulated independently. The **oxygen** tension of each **chamber** is regulated independently by adding **oxygen** , nitrogen, carbon dioxide, helium or another inert gas, or a mixture of two or more of the gases simultaneously with removing gas from the **chambers** , in the way that the pressure of the air is in accordance with the atmosphere. The pressure of the gases inside the **chambers** is slightly higher than the pressure of the atmosphere surrounding the main **chamber** . The humidity of each **chamber** is controlled and regulated to a level between 50 and 100 %. The entrance port and the exit port are combined to a single opening unit, such as a door. The entrance port and the exit port are

combined in a unit for transporting cell culturing units and equipment to and from the outer **chamber** . The combination of the entrance port and the exit port is an air lock. The entrance port constitutes an inner door of the air lock and the exit port constitutes an outer door of the air lock. The air lock comprises walls between the inner door and the outer door constituting a small **air - tight chamber** . The inner door and the outer door are opened one at a time in the way that only one door is open at a time, and the opening of one door sets going when the other door is totally shut. The atmosphere of the air lock is controlled and adjusted including contents of **oxygen** , nitrogen, carbon dioxide, helium or another inert gas, temperature and humidity. The inner door of the air lock opens only when the conditions including temperature, humidity and contents of **oxygen** is equal to the conditions inside the **chamber** which the air lock is positioned inside. A microscope is placed and used when handling (III), (V) and embryos. A working region is obtained within the main **chamber** , where the working region comprises a place for culturing cultured cell structures, where the cultured cell structure is observed in the microscope, and the working region comprises room for handling units. A micro-insemination apparatus is placed within the main **chamber** . The main **chamber** comprises an opening unit permitting entrance to human to handle the cell culture or the equipment inside the **chambers** . The opening unit is attached with gloves. The gloves are mounted in the way that human hands fit into the gloves and enable handling of the cell culture or the equipment inside the **chambers** . The opening unit is attached with sticks, bars or instruments manipulated by fiber optics, by which the cell culture or the equipment is handled. The main **chamber** has one or more small portion of its surface replaced with a membrane, where the membrane is sterile and has a structure through which a needle is stuck through, when the needle is removed the membrane fills up the region where the needle was stuck through, and no gases or particles diffuse through the membrane either when a needle is stuck through the membrane or no needle is stuck through the membrane. Two separate **chambers** are arranged as a main **chamber** and one or more smaller **air - tight** residence **chambers** . The smaller residence **chambers** are located inside the main **chamber** or are attached to the main **chamber** . The residence **chambers** are **air - tight** and are controlled independent of each other and independent of the main **chamber** according to temperature, humidity, and contents of **oxygen** , nitrogen and carbon dioxide, where the residence **chambers** constitute boxes for culture **containers** containing cell cultures of (III), (V), embryo, and (VII) including stem cell lines. Each box is adapted for receiving one culture **container** containing the cell cultures of (III), (V), embryo, and (VII) including stem cell lines. The number of the boxes correspond to the number of development stages of (III), (V), embryo and (VII) including stem cell lines. The development stages comprise at least immature, mature, fertilized (III), (V), 4 cell embryo, 8 cell embryo, morula, blastocyst and (VII) including stem cell lines. The **oxygen** tension and pressure of each **chamber** or **air - tight** boxes are regulated by a computer by retrieving an image of the embryo in the **chamber** or the **air - tight** boxes. The **air - tight** boxes are portable and when removed from (VI), is connected to units for controlling temperature, humidity and contents of **oxygen** , nitrogen and carbon dioxide. The unit for controlling temperature, humidity, and contents of **oxygen** , nitrogen and carbon dioxide is portable. The wall of the boxes contain a membrane. The small boxes

comprise fastening unit for fastening one or more cell culture **containers** . The wall of the cell culture **container** contains a sterile membrane. The small boxes are transported for at least 6 days. The size of the main **chamber** constitutes a room between 1 cm and 2 m of each wallBIOTECHNOLOGY - Preferred Method: In (M1), (III) and (V) are gametes obtained from female and male respectively, of a mammal such as cows, pigs, horses, goats, sheep, dogs, cats, rabbits, rats, mice, tigers, lions, pandas, gorilla, whales and humans, from cows, pigs, horses or preferably from humans. (III) is obtained from ovary or from primary and secondary ovarian follicles, pre-antral, early antral or antral follicles. (III) is obtained from the ovary by aspiration into a needle or by removing a portion of or the entire ovarian tissue containing primary, secondary or antral follicles and obtaining the primary, secondary or antral follicles from the ovarian tissue. The removed portion or the entire ovarian tissue is subjected to freezing. (III) is obtained from a mammal subsequent to treatment of the mammal with hormones capable of maturing (III), where the hormone is follicle-stimulating hormone (FSH) or luteinizing hormone (LH). (V) is matured or immatured comprising spermatids or spermatocytes, where (V) is obtained from testicular tissue removed from the male or from semen. (III) is immatured and obtained from a follicle. The follicle is 1-25, 2-18, 3-13, 5-12, 7-11 or 8-10 mm in diameter. The immatured gamete is in the prophase, dictyotene stage of first **meiotic** division or in the late stage of first **meiotic** metaphase. The culturing of the immature gamete up to metaphase II is associated with a synchronized cumulus, cytoplasm and nuclear maturation with a period of 20-30 hours. (III) and (V) are co-cultured with feeder-cells, resulting in fertilization of (III) by (V), where (III) is fertilized with (V) by intracytoplasmic sperm injection (ICSI). (III) and (V) are co-cultured for 50, 45, 40, 35, 30, 25, 20, 15, 10, 5, 4, 3, 2 hours, 1 hour, 30, 10, 5, 2 minutes or at least for 1 minute. The stage for transfer of the embryo is obtained by 9, 8, 7, 6, 5, 4, 3, 2, 1 or at least 1/2 day culture following fertilization of (III). The fertilized (III) is cultured to an embryo stage ready for transfer to the female uterus. The embryo stage is the two-cell, four-cell, six-cell, eight-cell, morula and blastocyst stages. In the embryo stage such as blastocyst stage, zona pellucida disappears. The zona pellucida of the embryo is opened to help the embryo hatch before implantation into the uterus, where the fragments of cell debris are removed from the embryo. The zona pellucida is opened by assisted hatching using laser, mechanical force or acid tyrode. The culturing conditions of (III), (V) and embryo comprise a temperature of 37 degreesC, and **oxygen** tension below 15%. The **oxygen** tension in the step of allowing cell-division is higher when compared to the **oxygen** tension in the culturing and the fertilizing steps. The **oxygen** tension is regulated in accordance to the phase and the condition of (III) or the embryo. The medium contains lipid or lipid precursors such as sterol or its functionally equivalent derivative. The medium among other factors contains aurin tricarboxylic acid (ATA), additives such as Medi-Cult SSR 4x, Medi-Cult SSR 4xa, Medi-Cult SSR 4xb, Medi-Cult SSR2 or Medi-Cult SSR3. If the culturing of the embryo result in an embryo at the 3-5 cell stage with 10-50 % fragmentation or less than 10 % fragmentation, then the embryo is awarded 6-7 points or 7-8 points, respectively in a cumulative embryo score (CES) scoring system. If the culturing of the embryo result in an embryo at the 4 cell stage with less than 10 % fragmentation, then the embryo is awarded 8 points in CES scoring system. The culturing of the

embryo result in an embryo of 7-9 cells 64-67 hours after fertilization to obtain a score of 60-100 according to the graduated embryo score (GES) scoring system. The culturing of the embryo result in an embryo of 7 cells, grade I or 8 cells, grade II or 9 cells, grade I 64-67 hours after fertilization to obtain a score of 70-100 or 80-100 according to the GES scoring system. In (M2), the embryo is transferred to the uterine tube of the female uterus, following a hormone treatment of the female. In (M3), the isolating, culturing and obtaining steps are carried out at an **oxygen** tension below 15 %.

Preferred Stem Cell: (VII) is stable indicating that no mutations or other genetic changes occur within the chromosomes or antigenicity on the surfaces of the cells

Derwent Class: B04; D16
International Patent Class (Main): C12N-005/06
International Patent Class (Additional): C12M-003/00; C12N-005/08

21/26,TI/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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015780375
WPI Acc No: 2003-842577/200378
Determining surface membrane protein populations, e.g. in studying cellular responses to stimuli, by forming complex with binding compound having cleavable linkage to eTag reporter

21/26,TI/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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015122043
WPI Acc No: 2003-182566/200318
Altering chromosomal sequence in a donor nucleus of a donor cell useful for producing recombinant organisms, by introducing a pair of single-stranded targeting polynucleotides and a recombinase into the donor nucleus of the donor cell

21/26,TI/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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013973200
WPI Acc No: 2001-457413/200149
Modifying chromosomal, non-chromosomal targets by enhanced homologous recombination using single stranded polynucleotide pair with homology clamp that is complementary to specific target DNA sequence, and recombinase

21/26,TI/5 (Item 5 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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013547644
WPI Acc No: 2001-031850/200104
New 14beta-H-sterol compounds are meiosis **inhibitors useful in contraception, without causing side effects on somatic cells observed with prior art estrogens and gestagens**

21/26,TI/6 (Item 6 from file: 350)

DIALOG(R)File 350:Derwent WPIX
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013393658
WPI Acc No: 2000-565596/200052
New 22R-hydroxycholesta-8,14-diene derivatives with meiosis inhibiting activity are useful in the control of fertility

21/26,TI/7 (Item 7 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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013387025
WPI Acc No: 2000-558963/200052
A method for producing transgenic rice plants

21/26,TI/8 (Item 8 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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013319337
WPI Acc No: 2000-491276/200043
New and known phosphonopyrazole compounds, useful as gametocides for inducing male sterility in plants and for producing hybrid seeds

21/26,TI/9 (Item 9 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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013052260
WPI Acc No: 2000-224115/200019
Novel method of performing transgenesis by coinsertion of nucleic acid and a nucleus into an unfertilized oocyte, used to produce transgenic animals

21/26,TI/10 (Item 10 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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009579279
WPI Acc No: 1993-272825/199334
Calmodulin-binding peptide(s) and derivs. - useful for inhibiting calmodulin, esp. in treatment of hyper proliferative diseases e.g. cancer

21/34/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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015241373
WPI Acc No: 2003-302299/200330
Delaying senescence of cells, useful for extending life of cultures, by appropriate selection of source cells and culture conditions
Patent Assignee: LAUTERBERG W (LAUT-I)
Inventor: LAUTERBERG W
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
DE 10130041	A1	20030116	DE 1030041	A	20010621	200330	B

Priority Applications (No Type Date): DE 1030041 A 20010621
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes

DE 10130041 A1 14 C12N-005/00
Abstract (Basic): DE 10130041 A1

NOVELTY - Retarding senescence of cells which exhibit senescence-specific markers (SSM) with sequences that originate in the line of inheritance from source cells, is new.

DETAILED DESCRIPTION - Retarding senescence of cells which exhibit senescence-specific markers (SSM) with sequences that originate in the line of inheritance from source cells. The method establishes a final increase in polymorphisms in SSM that is indicative of the onset of senescence by choosing source cells with selected sequences for SSM and/or selecting culture conditions, and heterochromatization of SSM, in appropriately extended cell cycle times, for the appropriate number of cell divisions.

USE - The method is used to extend the life of cultures.

pp; 14 DwgNo 0/0

Technology Focus:

TECHNOLOGY FOCUS - BIOLOGY - Preferred Cells: These are Ascomycetes or Chordata, especially mammalian, and are then stem cells (of any origin) or differentiated somatic cells, and they may be produced from cultured precursor cells. The line of inheritance may be mitotic or **meiotic** . The markers are highly or moderately repetitive sequences and/or senescence-specific genes, particularly (extra)chromosomal sequences that contain ARS elements. Suitable highly repetitive sequences are 5-60 bp microsatellites; 10-2000 bp palindromes; 250-15000 bp Scaffold attachment region (SAR) elements; 100-5000 bp Short interspersed nuclear element (SINE) sequences; 5000-70000 bp Long Interspersed Nuclear Elements (LINE) sequences and/or telomeric repeats. The moderately repetitive sequences are tandem repeats of genes for rRNA and/or histones; and/or V-gene segments of immunoglobulins and/or T cell receptor sequences. Senescence-specific genes are the Saccharomyces cerevisiae genes CDC, UTH, SGS, SIR or RAD or their mammalian analogs, and they contain methylated CpG islands.

Preferred Process: To determine a suitable cell source with selected SSM, the mean number of cell divisions in test cells from different sources (of the same cell type) that occur before proliferation ceases is determined in complete medium. The sources with the lowest and highest number of divisions are chosen and the differences between (extra)chromosomal sequences in them are determined. Suitable culture conditions are atmosphere (content of **oxygen** and carbon dioxide; pressure and temperature); energy and metabolite sources (e.g fatty acids, proteins and sugars); added factors (e.g. growth factors or carnosine); and presence of agents that affect distribution of nutrients (e.g. surfactants). To select these conditions, cells of a source with the lowest number of divisions before the end of proliferation are grown under various conditions then differences in (extra)chromosomal sequences determined. Heterochromatization of SSM is reduced through selected sequence groupings, especially DNaseI-hypersensitive sites; promoters, enhancers and/or locus control regions; sequences preceded or followed by polyoma virus or simian virus 40 sequences; and non-methylated CpG islands (where demethylated by adding a steroid). The donor of the cell source is selected to have a degree of heterozygosity at gene loci of SSM 0-0.3, especially 0-0.15, where these loci are the S. cerevisiae genes listed above, or their mammalian analogs, and/or rRNA genes.

Extension Abstract:

EXAMPLE - None given.

Derwent Class: B04; D16
International Patent Class (Main): C12N-005/00
International Patent Class (Additional): C12Q-001/02; C12Q-001/68

32/26,TI/12 (Item 12 from file: 350)
DIALOG(R)File 350:Derwent WPIX

011802159
WPI Acc No: 1998-219069/199820
Preserving **acarbose or acarbose-containing preparations - by keeping in hermetically** sealed **, moisture proof** containers **in** absence **of** oxygen

32/26,TI/14 (Item 14 from file: 350)
DIALOG(R)File 350:Derwent WPIX

010265929
WPI Acc No: 1995-167184/199522
Aminoacid infusion prepn. in plastic container - comprising tryptophan in container sealed **with gas material in presence of deoxidant, prevents bronchospasm or anaphulactic shock**

32/26,TI/21 (Item 1 from file: 347)
DIALOG(R)File 347:JAPIO

07363306
SUBSTRATE TRANSFER **CONTAINER** , OPENING/ **CLOSING** APPARATUS FOR SUBSTRATE TRANSFER CONTAINER, AND METHOD FOR **STORING** SUBSTRATE

32/34/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016027736
WPI Acc No: 2004-185587/200418
Method for stabilizing growth hormone in formulation containing growth hormone powder and lactose powder, by sealing **formulation in** container **of gas barrier property with desiccant and deoxidizing agent**
Patent Assignee: JAPAN CHEM RES CO LTD (NICH-N)
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
JP 2004051502	A	20040219	JP 2002208269	A	20020717	200418	B

Priority Applications (No Type Date): JP 2002208269 A 20020717
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
JP 2004051502	A		15	A61K-038/27	

Abstract (Basic): JP 2004051502 A

NOVELTY - A method for stabilizing growth hormone in formulation containing growth hormone powder and lactose powder, involves sealing formulation in a container of gas barrier property with desiccant and deoxidizing agent or with substance having drying effect and deoxidizing effect, in a state which prevent the direct contact of formulation with desiccant and deoxidizing agent or with substance.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for growth hormone containing powder formulation.

USE - For stabilizing growth hormone in formulation.
ADVANTAGE - The growth hormone containing powder formulation has excellent storage stability for long period of time.
pp; 15 DwgNo 0/0
Technology Focus:
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The lactose powder is spray-dried lactose and anhydrous lactose. The lactose powder has moisture content of 1% or less. The growth hormone powder is vacuum -dried powder.
Derwent Class: B04; B07; P33; Q34
International Patent Class (Main): A61K-038/27
International Patent Class (Additional): A61J-001/03 ; A61K-009/14; A61K-009/19; A61K-009/72; A61K-047/26; A61P-005/06; A61P-011/00; A61P-011/06; B65D-081/26

33/26,TI/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
017046421
WPI Acc No: 2005-370744/200538
Screening for oxysterol that activates LXR alpha mediated transcription, by introducing reporter construct and human LXR alpha expression construct into host cell and treating host cell with oxysterol activator of LXR alpha

33/26,TI/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
015902339
WPI Acc No: 2004-060179/200406
Novel transducer of meiosis activating sterols **designated SAM1a and SAM1b useful for screening for agonist or antagonist of** meiosis activating sterols **used to treat infertility or to provide a way of contraception**

33/26,TI/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
015459621
WPI Acc No: 2003-521763/200349
Nucleic acids encoding membrane receptors for steroids or sterols, useful for identifying modulators of a pgk polypeptide, as a target substance for the production of an agent for steroid hormone-dependent diseases, e.g. infertility

33/26,TI/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
015081300
WPI Acc No: 2003-141818/200314
New nucleic acid encoding human receptor for steroid or sterol, useful for identifying modulators, for treating e.g. osteoporosis and prostatic hypertrophy

33/26,TI/5 (Item 5 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
014789557
WPI Acc No: 2002-610263/200266
Use of potent inhibitors to increase the concentration of sterols in the cholesterol synthesis for the control of fertility

33/26,TI/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
014269151
WPI Acc No: 2002-089849/200212
Use of meiosis - activating substance **in culture medium for in vitro fertilization of aged oocytes or for preparation of medicament for use in** fertilization of aged oocytes

33/26,TI/7 (Item 7 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
014196705
WPI Acc No: 2002-017402/200202
Use of nuclear maturation inhibiting substance and gonadotropin and/or growth factor for preparation of a cell culture medium for in vitro maturation of oocytes

33/26,TI/9 (Item 9 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
013781784
WPI Acc No: 2001-265995/200127
Solid composition comprising meiosis activating substance **and an additive, useful for in-vitro fertilization**

33/26,TI/10 (Item 10 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
013415367
WPI Acc No: 2000-587305/200055
Use of culture medium comprising meiosis activating sterol **or an additive such as gonadotropin and growth hormone for improving the viability and pregnancy** potential of in vitro oocyte fertilization

33/26,TI/11 (Item 11 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
011109390
WPI Acc No: 1997-087315/199708
New 18-nor-cholesta-8,11,13-triene and 8,11,13,24-tetraene cpds., used to regulate meiosis - useful as contraceptives without side effects of hormonal based contraceptives and in treatment of infertility

33/26,TI/12 (Item 12 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
010928469
WPI Acc No: 1996-425420/199642

Stimulating meiosis of oocytes and male germ cells - by administering cpd. causing accumulation of endogenous meiosis activating substance **to level at which meiosis is induced, for use in regulating fertility**

33/34/8 (Item 8 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013871711
WPI Acc No: 2001-355923/200137
Improved in vitro fertilization process for treating human infertility, comprises actively arresting oocyte and subsequently reversing the arrest and fertilizing the oocyte, to form meiotic stimulating molecules
Patent Assignee: NOVO NORDISK AS (NOVO); GRONDAHL C (GRON-I)
Inventor: GRONDAHL C
Number of Countries: 095 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200138493	A1	20010531	WO 2000DK647	A	20001123	200137	B
AU 200116929	A	20010604	AU 200116929	A	20001123	200153	
EP 1235899	A1	20020904	EP 2000979451	A	20001123	200266	
			WO 2000DK647	A	20001123		
US 6544166	B1	20030408	US 2000241806	P	20001018	200327	
			US 2000718710	A	20001122		
JP 2003514580	W	20030422	WO 2000DK647	A	20001123	200336	
			JP 2001540246	A	20001123		

Priority Applications (No Type Date): DK 991705 A 19991125
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200138493	A1	E	18	C12N-005/00	
	Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW				
	Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW				
AU 200116929	A			C12N-005/00	Based on patent WO 200138493
EP 1235899	A1	E		C12N-005/00	Based on patent WO 200138493
	Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR				
US 6544166	B1			A61D-019/00	Provisional application US 2000241806
JP 2003514580	W		22	C12N-005/06	Based on patent WO 200138493

Abstract (Basic): WO 200138493 A1

NOVELTY - An in vitro fertilization process comprising arresting oocyte removed from a woman, reversing the arrested state and fertilizing the oocyte, provided that from the moment of oocyte removal and in the following 16 hours, no spontaneous maturation visualized as early germinal vesicle breakdown (GVB), or no GVB appears, before inducing meiosis by **meiosis activating substance** (MAS), is new.

DETAILED DESCRIPTION - An in vitro fertilization process comprising arresting oocyte removed from a woman, reversing the arrested state and fertilizing the oocyte, provided that from the moment of oocyte removal and in the following 16 hours, preferably the following hour, no spontaneous maturation visualized as early germinal vesicle breakdown (GVB), or no GVB appears, before inducing meiosis by **meiosis activating substance** (MAS), is new.

ACTIVITY - Antiinfertility. Oocytes were obtained from immature female mice (C57BI/6JxDBA/2J F1 hybrids), and cultured under different culture conditions. First group (control) included no inhibition and no follicular fluid- **meiosis activating substance** (FF-MAS), second group included no inhibition and 10 M FF-MAS, third group (inhibition and spontaneous maturation) included culturing in Hx-medium for 4 hours and then in Hx-free medium, and fourth group (inhibition and FF-MAS induction) included culturing in Hx medium for 4 hours and addition of FF-MAS to Hx medium. In vitro fertilization was followed after 16-20 hours maturation. Fertilization rate was found to 75% and embryo development rate was found to be 30% for the fourth treatment group, whereas the values were found to be less than 50% and less than 10% respectively, for the other treatment groups.

MECHANISM OF ACTION - None given.

USE - The method is useful for treating human infertility.

pp; 18 DwgNo 0/0

Technology Focus:

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method further involves allowing the oocyte to develop after fertilization. The conditions where the arrested state is reversed are brought about using a MAS, or culture conditions leading to endogenous formation of meiotic stimulating molecules in the oocyte-cumulus complex.

Extension Abstract:

ADMINISTRATION - No administration details given.

EXAMPLE - Oocytes were aspirated under sedation through ultrasound guided transvaginal follicle aspiration of middle to large sized follicles, from female patient after performing gynecological investigation in the subject. After the removal of an oocyte from the meiosis inhibitory milieu a patient's follicle, the oocyte was subjected to conditions causing the oocyte to maintain meiotic arrest, or avoid spontaneous maturation of the oocyte. The conditions involved culturing cumulus enclosed oocytes together in co-culture with cumulus cells/granulosa cells, or by adding the physiological phosphodiesterase enzyme (PDE) inhibitor hypoxanthine to the medium in a concentration of 3 mM. After 1 hour in medium TCM (undefined)-199 including granulosa cells and hypoxanthine to ensure meiotic arrest, 20 microM of follicular fluid- **meiosis activating substance** (FF-MAS) was added to the medium, which was then cultured for 24 hours at 37.4 degrees C to overcome the meiotic arrest.

Derwent Class: B04; D16; P32
International Patent Class (Main): A61D-019/00; C12N-005/00; C12N-005/06
International Patent Class (Additional): A61K-031/56; A61K-035/52; A61K-035/54; A61P-015/08

38/26,TI/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

017022222
WPI Acc No: 2005-346539/200535
Inducing stasis in one or more cells separated from an organism, useful to preserve cells, comprises identifying the cell(s) in which stasis is desired and exposing the cell(s) to an oxygen antagonist to induce stasis

39/26,TI/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

017031686
WPI Acc No: 2005-356004/200536
Inducing stasis in in vivo biological matter comprises exposure of the organism to an oxygen antagonist

39/26,TI/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016971685
WPI Acc No: 2005-295998/200530
Determining the suitability of unfertilized oocyte **, for** storage **or for use in fertility or reproductive treatment, comprises providing the first polar body associated with or derived from the unfertilized** oocyte

39/26,TI/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016838954
WPI Acc No: 2005-163237/200517
Preserving **a biomaterial, e.g. hepatocytes, comprises exposing a biomaterial having a membrane and transporter molecule to a** preservation **agent**

39/26,TI/5 (Item 5 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016662408
WPI Acc No: 2004-821127/200481
Preserving **viability of living biological material such as heart, kidney, lung, liver, embryo, platelets, in solution having trimethyl amine oxide, calcium ions and sodium chloride, and free of iodide, dihydrogen phosphate, bicarbonate**

39/26,TI/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016598153
WPI Acc No: 2004-756887/200474
Preparing a spermatozoon for use in intracytoplasmic sperm injection-mediated transgenesis, comprises suspending spermatozoon, treating to obtain demembranated spermatozoon and incubating with exogenous nucleic acid

39/26,TI/7 (Item 7 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016497516
WPI Acc No: 2004-655462/200464
Oocyte **recovery apparatus for removing** oocytes **from female patient, includes self-contained unit with connectors, receptacle for collecting** oocytes **,** oocytes **supplying mechanism, flushing liquid supply line, and selector**

39/26,TI/8 (Item 8 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015939350
WPI Acc No: 2004-097191/200410
Spermatozoa or sperm heads freezing or freezing-drying composition comprising a buffered medium and an ion-chelating agent, which enables the spermatozoa or sperm heads to maintain chromosome integrity at wide temperature range

39/26,TI/9 (Item 9 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015913438
WPI Acc No: 2004-071278/200407
New polymeric based complex useful for retaining cellular viability comprises comonomer, saccharide residue and lipid metabolite

39/26,TI/10 (Item 10 from file: 350)
DIALOG(R)File 350:Derwent WPIX

015893148
WPI Acc No: 2004-050983/200405
Solution for preserving **living biological materials e.g. organs, tissues and cells for use in transplantation, has betaine, sodium chloride and sodium citrate and is isotonic with biological material to be** preserved

39/26,TI/11 (Item 11 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014406734
WPI Acc No: 2002-227437/200229
Aspiration of oocytes **from bovine ovaries uses improvised apparatus consisting of** vacuum **pump for creating negative pressure within aspiration system, safety trap and collecting container connected to pump at opposite ends**

39/26,TI/12 (Item 12 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014234931
WPI Acc No: 2002-055629/200207
Cryopreservation of a cell in a dormant state, comprises microinjection **of a sugar protective agent followed by treatment to induce the dormant state**

39/26,TI/13 (Item 13 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013506720
WPI Acc No: 2000-678664/200066
Storage **system for cryopreservation of small cells such as sperm cells, comprising sperm precursor cells or spermatozoa, disposed inside mammalian zona pellucida**

39/26,TI/14 (Item 14 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013192538
WPI Acc No: 2000-364411/200031
Preservation of biological materials, such as platelets, platelet membranes, involves lyophilization of biological material after contacting it with preservative solution

39/26,TI/15 (Item 15 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013133784
WPI Acc No: 2000-305655/200027
Novel hydrophilic Eimeria polypeptides comprise sequences with at least 70% homology with sequences of 13-223 amino acids, useful as vaccines against Coccidosis in poultry

39/26,TI/16 (Item 16 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012784747
WPI Acc No: 1999-590973/199950
New freeze - dried spermatozoa which, when rehydrated, can be used to fertilize oocytes and produce live offspring

39/3,K/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

017071118
WPI Acc No: 2005-395459/200540
Related WPI Acc No: 2005-346539; 2005-356004
XRAM Acc No: C05-122269
XRPX Acc No: N05-320538
Use of oxygen antagonist for inducing stasis in isolated tissues e.g. tissues of circulatory system, to preserve tissues ex vivo for research and diagnostic applications
Patent Assignee: HUTCHINSON CANCER RES CENT FRED (HUTC-N)
Inventor: ROTH M B
Number of Countries: 108 Number of Patents: 001
Patent Family:
Patent No Kind Date Applicat No Kind Date Week
WO 200541656 A2 20050512 WO 2004US35034 A 20041022 200540 B
Priority Applications (No Type Date): US 2004577942 P 20040608; US 2003513458 P 20031022; US 2004548150 P 20040226
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200541656 A2 E 114 A01N-001/02
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
Abstract (Basic):

... gland, thyroid gland, lung, retina, kidney, and umbilical cord) from mammals (e.g. human) to **preserve** tissue ex vivo (claimed), which are useful in transplantation, research purpose and diagnostic applications...
Technology Focus:
... cornea), stem cell (cord blood or umbilical cord, bone marrow, or embryonic), unfertilized or fertilized **oocyte** , or sperm...
...or oxidative phosphorylation in the tissue; removing the oxygen antagonist; placing the tissue under a **vacuum** ; increasing the ambient temperature relative to the reduced temperature when the tissue achieves a core...
...container rests; a pressure regulator that regulates the pressure inside the sample chamber; and a **vacuum** unit or structure configured to provide a **vacuum** . The gas regulators can be electronically programmed to control, for a specified period, the amount...
Extension Abstract:
... Human foreskin tissues were **preserved** in keratinocyte growth medium containing insulin, endothelial growth factor (0.1 ng/ml), hydrocortisone (0...
...growth, whereas keratinocytes in test chamber showed significant growth. The results showed that 100 % CO2 **preserved** human skin efficiently even at room temperature.

43/26,TI/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
016870691
WPI Acc No: 2005-194996/200520
Amino derivatives are cholesterol ester transfer protein inhibitors useful to treat or prevent e.g. coronary artery diseases and dyslipidemia

43/26,TI/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
013816061
WPI Acc No: 2001-300273/200131
Producing liposome preparation, having excellent action and redispersion in aqueous medium, by vacuum **drying liposome condensed solution without freezing while bubbling or after bubbling condensed solution**

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L1             5 S E4 OR E5 OR E6 OR E7 OR E11
                E MEIOSIS INDUCING/CN
L2             2 S E5 OR E6
                E MEIOSIS-ACTIVATING
                E MEIOSIS-ACTIVATING/CN
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     FILE 'REGISTRY' ENTERED AT 11:53:44 ON 12 JUL 2005
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L3             1 S E3
                E O2/CN
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L4           100 S L1 OR L2 OR MEIOSIS()(ACTIVAT? OR INDUC?)()(STEROL# OR
SUBSTA
L5        823747 S L3 OR OXYGEN OR O2
L6       4502847 S LOW OR LOWER OR REDUCED OR ABSENCE OR MINOR
L7            81 S (MOLE OR MOLES)(1W)(LITER OR LITRE)
L8        601009 S STORE# OR STORING OR STORAGE OR PRESERV?
L9             2 S L4 AND L5 [2 duplicates]
L10            2 S L4 AND L8
L11            2 S L10 NOT L9 [not relevant]
     FILE 'BIOTECHNO' ENTERED AT 11:59:41 ON 12 JUL 2005
L12            1 S L4 AND L5 [a duplicate]

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         (c) format only 2005 The Dialog Corp.
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         (c) 2005 BIOSIS
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         (c) 2005 Elsevier Science Ltd.
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         (c) 2005 The HW Wilson Co.
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         (c) 2005 BLDSC all rts. reserv.
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Set     Items   Description
S1      57822   MEIOSIS()(ACTIVAT? OR INDUC???)()(SUBSTANCE? ? OR STEROL? -
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S3     436657   VACUO OR VACUUM
S4      59925   FREEZE()(DRY??? OR DRIES OR DRIED)
S5        843   (MOLE OR MOLES)(1W)(LITER OR LITRE)
S6   15548281   LOW OR LOWER OR REDUCED OR ABSENCE OR MINOR
S7    1915501   CONTAINER? ? OR CHAMBER? ? OR RECEPTACLE? ? OR CANISTER? ?
            OR VESSEL? ? OR VIAL? ? OR CAPOUL? ? OR DISH OR DISHES
S8     362481   SEAL?? OR SEALING OR ENCLOS????
S9    1742740   CLOSE OR CLOSES OR CLOSED OR CLOSING OR AIRTIGHT OR AIR()T-
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S10   2600548   STORE? ? OR STORING OR STORAGE OR PRESERV?
S11     89965   VITRO()(FERTILI?ATION OR MATURATION) OR IVF OR IVM
S12     36604   S6()S2
S13     65968   S6(2W)S2
S14         6   S2(5N)S5
S15     31313   S8:S9(3N)S7
S16         0   S1 AND S12 AND S15
S17         0   S1 AND S13:S14 AND S15
S18        41   S1 AND S12
S19       110   S1 AND S13:S14
S20        24   S10 AND S18:S19
S21         0   S11 AND S20
S22        11   RD S20 (unique items)
S23         4   S22/2002:2005
S24         7   S22 NOT S23
S25         7   Sort S24/ALL/PY,A [not relevant]
S26       579   MEIOSIS()(ACTIVAT? OR INDUC???)()(SUBSTANCE? ? OR STEROL? ?)
S27         8   S26 AND S2:S3
S28         4   RD (unique items)
S29         0   S26 AND S4
S30       610   STEROL? ? AND (MEIOSIS OR MEIOTIC)
S31         8   S30 AND S2:S4
S32         2   S31 NOT (S20 OR S27)
S33         2   RD (unique items) [not relevant]
```

S34 95368 MEIOSIS
S35 450 S34 AND S2:S4
S36 24 S34 AND S12:S14
S37 24 S36 NOT (S20 OR S27 OR S31)
S38 13 RD (unique items)
S39 3 S38/2002:2005
S40 10 S38 NOT S39
S41 10 Sort S40/ALL/PY,A
S42 127073 STEROL? ?
S43 129 S42 AND S12:S14
S44 16 S10 AND S43
S45 16 S44 NOT (S20 OR S27 OR S31 OR S36)
S46 7 RD (unique items)
S47 7 Sort S46/ALL/PY,A [not relevant]
S48 6 S43 AND S7:S9
S49 6 S48 NOT (S20 OR S27 OR S31 OR S36 OR S44)
S50 2 RD (unique items) [not relevant]

28/7/2 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.
0005357468 BIOSIS NO.: 198732086359
MATURATION OF MURINE DICTYATE OOCYTES IN-VITRO INFLUENCE OF PH FLUCTUATIONS DURING OOCYTE ISOLATION OXYGEN **TENSION DURING ISOLATION AND CULTURE THE** MEIOSIS INDUCING SUBSTANCE **MIS AND THE MEIOSIS PREVENTING SUBSTANCE MPS**
AUTHOR: BAGGER P V (Reprint); BYSKOV A G; CHRISTENSEN M
AUTHOR ADDRESS: DEP GYNEC AND OBST, HVIDOVRE HOSPITAL, DENMARK**DENMARK
JOURNAL: Human Reproduction (Oxford) 1 (SUPPL. 2): p37-38 1986
CONFERENCE/MEETING: SECOND MEETING OF THE EUROPEAN SOCIETY OF HUMAN REPRODUCTION AND EMBRYOLOGY. HUM REPROD (OXFORD).
ISSN: 0268-1161
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

41/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2005 BIOSIS. All rts. reserv.
0002208513 BIOSIS NO.: 197764056869
CHANGES OF X-RAY SENSITIVITY OF TRILLIUM CHROMOSOME DURING MEIOSIS **WITH SPECIAL REFERENCE TO EFFECTS OF NITROGEN GAS AND CARBON MON OXIDE ON THE SENSITIVITY**
AUTHOR: KANAZAWA H
JOURNAL: Journal of the Faculty of Science Hokkaido University Series V Botany 10 (4): p245-280 1977
ISSN: 0368-2145
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Unspecified
ABSTRACT: The change of radiosensitivity of chromosomes during **meiosis** in PMC [pollen mother cells] of T. kamtschaticum Pall and the modifying effect of N2 and CO on the sensitivity were studied. Chromosome aberrations induced by X-ray irradiation were used as a measure of the sensitivity. PMC at zygotene, pachytene and diplotene were irradiated

with X-rays (30 R), and radiosensitivity was estimated by scoring induced isochromatid breaks, chromatid breaks, minute acentric fragments and exchange type aberrations at the 1st metaphase. Cells at pachytene showed relatively high sensitivity for X-rays. The N2 treatment largely reduced aberration yield at all 3 stages tested, without delay of the division process. The reducing effect of N2 and CO was highest at late pachytene. To estimate radiosensitivity of chromosomes at different stages during **meiosis** , an index showing relative sensitivity was required. Experiments were performed to choose a reliable standard of micronuclei at tetrad, dwarf pollen and pollen mitosis metaphase stages. The frequency of fragments appearing at the microspore metaphase was used as the standard of radiosensitivity of chromosomes during meiotic cycle. Plotting sensitivity during the meiotic cycle showed a roughly bimodal curve having 1 major peak at the 1st metaphase and a minor peak at the 2nd metaphase. The sensitivity of prophase cells showed an irregular curve dropping down at mid-pachytene and having a small peak at late-pachytene. Chromosome aberrations, produced by X-raying at the 1st metaphase and observed at the microspore metaphase, were reduced to about half by the N2 treatment prior to and after irradiation. N2 was effective at pachytene. CO reduced chromosome aberrations induced by X-rays. Treatments of X-rays, N2 and CO in various combinations reduced the frequency of aberrations more than X-ray irradiation in N2 or CO. N2 and CO **reduced** **O2** in cells by gas exchange, affecting the occurrence of chromosome breaks by X-rays and the rejoining system. Inhibition of respiration by N2 and CO prevented the movement of chromosomes and the rejoining of breaks, so that break ends did not form exchange type aberrations but remained capable of restitution.

41/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0003238389 BIOSIS NO.: 198171057348
ALLOMYCES-NEOMONILIFORMIS GAMETOGENESIS THE CYSTOGENES LIFE CYCLE
AUTHOR: OLSON L W (Reprint)
AUTHOR ADDRESS: INST GENETICS, UNIV COPENHAGEN, OSTER FARIMAGSGADE 2A, DK-1353 COPENHAGEN K, DENMARK**DENMARK
JOURNAL: Protoplasma 105 (1-2): p87-106 1980
ISSN: 0033-183X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH
ABSTRACT: In A. neomoniliformis **meiosis** takes place during resting sporangium germination. Meiospores are characteristically binucleate and biflagellate. Variation in number of nuclei and flagella per meiospore from two was correlated with germination of the resting sporangia under **reduced** **O2** tension. Meiospores were extremely poor swimmers and typically amoeboid. At encystment, the gamma bodies of the cell were mobilized and appear involved in cyst wall synthesis. A single mitotic division of each nucleus gives rise to 4 nuclei. Assembly of the nuclear cap and side body complex of the spore were extremely late processes in gametogenesis. Gametes were released when the single papilla dissolves. Gametes fuse in pairs and after zygote formation the cell is uninucleate with 2 flagella. The biflagellate zygote is an active swimming cell. Presence of homothallism or heterothallism in A. neomoniliformis was discussed.

41/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011042792 BIOSIS NO.: 199799676852
Reduced oxygen tension inhibits in-vitro maturation of squirrel monkey oocytes
AUTHOR: Yeoman R R (Reprint); Williams L E; Abee C R
AUTHOR ADDRESS: Dep. Obstet. Gynecol., Univ. South Ala., Mobile, AL 36688, USA**USA
JOURNAL: Biology of Reproduction 56 (SUPPL. 1): p96 1997 1997
CONFERENCE/MEETING: Thirtieth Annual Meeting of the Society for the Study of Reproduction Portland, Oregon, USA August 2-5, 1997; 19970802
ISSN: 0006-3363
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

41/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13305952 PMID: 10079414
Low oxygen **inhibits but complex high-glucose medium facilitates in vitro maturation of squirrel monkey** oocyte-granulosa cell complexes.
Yeoman R R; Williams L E; Abee C R
Department of Obstetrics/Gynecology, University of South Alabama, Mobile 36608, USA.
Journal of assisted reproduction and genetics (UNITED STATES) Feb 1999, 16 (2) p102-7, ISSN 1058-0468 Journal Code: 9206495
Contract/Grant No.: P40 RR01254; RR; NCRR
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
PURPOSE: The objectives of these in vitro maturation studies in primate cumulus-oocyte complexes (COCs) were to evaluate the effect of a **reduced - oxygen** environment and to compare medium with a high-glucose concentration to medium with pyruvate but no glucose. METHODS: COCs were retrieved from squirrel monkeys stimulated with 1 mg of follicle-stimulating hormone (FSH) for 4-6 days. Experiment 1 examined maturation after 48 hr in 5% O2/5% CO2/90% N2 compared with 5% CO2/air. The medium was CMRL-1066 containing moderate glucose (5.5 mM) supplemented with 1 mM glutamine, 0.33 mM pyruvate, 0.075 IU/ml human FSH, 5 IU/ml human chorionic gonadotropin, 75 U penicillin G/ml, and 20% fetal bovine serum. Experiment 2 in 5% CO2/air, compared P-1 medium (pyruvate and lactate but no glucose) to Waymouth's medium (27.5 mM glucose), both with identical supplements. RESULTS: Only 3 (8%) of 37 COCs matured in 5% O2, while 39 (49%) of 80 matured in ambient O2. Fourteen (22%) of 64 complexes matured in P-1 medium, compared to 47 (49%) of 96 **meiosis** II oocytes in Waymouth's medium ($P < 0.05$). CONCLUSIONS: These are the first primate studies showing **detrimental effects of reduced - oxygen culture on in vitro maturation.** Additionally, maturation was enhanced with complex high-glucose medium suggesting that the predominant metabolism is aerobic

glycolysis.
Record Date Created: 19990601
Record Date Completed: 19990601

41/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13092820 PMID: 11066064
Low oxygen **tension during in vitro maturation is beneficial for supporting the subsequent development of bovine cumulus-oocyte complexes.**
Hashimoto S; Minami N; Takakura R; Yamada M; Imai H; Kashima N
Embryo Transplantation Laboratory, Snow Brand Milk Products Co. Ltd., Tomakomai, Hokkaido, Japan. snowet@coral.ocn.ne.jp
Molecular reproduction and development (UNITED STATES) Dec 2000, 57 (4) p353-60, ISSN 1040-452X Journal Code: 8903333
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The effects of carbohydrates on meiotic maturation and ATP content of bovine oocytes under **low oxygen** tension (5%) were investigated. Furthermore, the developmental competence or intracellular H(2)O(2) contents of the oocytes matured under 5% or 20% O(2) was assessed. In vitro maturation of bovine cumulus-oocyte complexes was performed in synthetic oviduct fluid (SOF) containing 20 amino acids and hormones (SOFaa). The proportion of the oocytes that matured to the metaphase II stage in SOFaa containing 1.5 mM glucose, 0.33 mM pyruvate, and 3.3 mM lactate under 5% O(2) was dramatically lower than that of oocytes matured under 20% O(2) ($P < 0.01$). Similarly, the ATP content of the oocytes that matured under 5% O(2) was much lower than that of oocytes matured under 20% O(2) ($P < 0.05$). Under 5% O(2) the proportion of metaphase II oocytes increased with increasing glucose concentration (0-20 mM) in SOFaa without pyruvate or lactate. In addition, the ATP content of oocytes cultured in 20 mM glucose was higher ($P < 0.05$) than that of oocytes cultured in 1. 5 mM glucose. Two glucose metabolites (pyruvate and lactate) and a nonmetabolizable glucose analog (2-deoxy-glucose), however, had no noticeable effects on meiotic maturation under 5% O(2). These results suggest that ATP production under 5% O(2) is not dependent on the TCA cycle. Addition of iodoacetate, a glycolytic inhibitor, to SOFaa containing 20 mM glucose significantly reduced ($P < 0.01$) the proportion of metaphase II and ATP content. Moreover, the proportion of the development to the blastocyst stage of oocytes matured under 5% O(2) was higher ($P < 0.05$) than that of oocytes matured under 20% O(2). H(2)O(2) contents of oocytes matured under 5% O(2) was lower ($P < 0.05$) than that of oocytes matured under 20% O(2). The results of the present study demonstrate that glucose plays important roles in supporting the completion of meiotic maturation in bovine cumulus-oocyte complexes under **low oxygen** tension and that **low oxygen** tension during in vitro maturation is beneficial for supporting the subsequent development of bovine oocytes.
Record Date Created: 20001211
Record Date Completed: 20001211

```
File  20:Dialog Global Reporter 1997-2005/Jul 12
         (c) 2005 The Dialog Corp.
Set     Items   Description
S1          2   MEIOSIS()(ACTIVAT? OR INDUC???)()(SUBSTANCE? ? OR STEROL? ?)
[not relevant]
S2      75621   OXYGEN OR O2
S3      66604   VACUO OR VACUUM
S4       2147   FREEZE()(DRY??? OR DRIES OR DRIED)
S5          3   (MOLE OR MOLES)(1W)(LITER OR LITRE)
S6    4743334   LOW OR LOWER OR REDUCED OR ABSENCE OR MINOR
S7    1007073   CONTAINER? ? OR CHAMBER? ? OR RECEPTACLE? ? OR CANISTER? ?
             OR VESSEL? ? OR VIAL? ? OR CAPOUL? ? OR DISH OR DISHES
S8     342771   SEAL?? OR SEALING OR ENCLOS????
S9    4298330   CLOSE OR CLOSES OR CLOSED OR CLOSING OR AIRTIGHT OR AIR()T-
            IGHT OR HERMETIC?
S10   2274039   STORE? ? OR STORING OR STORAGE OR PRESERV?
S11     12042   VITRO()(FERTILI?ATION OR MATURATION) OR IVF OR IVM
S12      1316   MEIOSIS OR STEROL? ?
S13         0   S12(S)S2:S4
S14        21   S12 AND S2:S4
S15        18   RD (unique items)
S16        10   S15/2002:2005
S17         8   S15 NOT S16
S18         8   Sort S17/ALL/PD,A [not relevant]

File  98:General Sci Abs/Full-Text 1984-2004/Dec
         (c) 2005 The HW Wilson Co.
File 135:NewsRx Weekly Reports 1995-2005/Jul W1
         (c) 2005 NewsRx
File 369:New Scientist 1994-2005/May W2
         (c) 2005 Reed Business Information Ltd.
File 370:Science 1996-1999/Jul W3
         (c) 1999 AAAS
File  16:Gale Group PROMT(R) 1990-2005/Jul 11
         (c) 2005 The Gale Group
File 160:Gale Group PROMT(R) 1972-1989
         (c) 1999 The Gale Group
File 148:Gale Group Trade & Industry DB 1976-2005/Jul 12
         (c)2005 The Gale Group
File 621:Gale Group New Prod.Annou.(R) 1985-2005/Jul 12
         (c) 2005 The Gale Group
File   9:Business & Industry(R) Jul/1994-2005/Jul 11
         (c) 2005  The Gale Group
File 149:TGG Health&Wellness DB(SM) 1976-2005/Jul W1
         (c) 2005 The Gale Group
File 129:PHIND(Archival) 1980-2005/Jul W1
         (c) 2005 T&F Informa UK Ltd
File 481:DELPHES Eur Bus 95-2005/Jul W1
         (c) 2005 ACFCI & Chambre CommInd Paris
File 624:McGraw-Hill Publications 1985-2005/Jul 11
         (c) 2005 McGraw-Hill Co. Inc
File 635:Business Dateline(R) 1985-2005/Jul 09
         (c) 2005 ProQuest Info&Learning
File 636:Gale Group Newsletter DB(TM) 1987-2005/Jul 11
         (c) 2005 The Gale Group
Set     Items   Description
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S1          30   MEIOSIS()(ACTIVAT? OR INDUC???)()(SUBSTANCE? ? OR STEROL? ?)
S2      207131   OXYGEN OR O2
S3      166304   VACUO OR VACUUM
S4        8076   FREEZE()(DRY??? OR DRIES OR DRIED)
S5          75   (MOLE OR MOLES)(1W)(LITER OR LITRE)
S6     6720233   LOW OR LOWER OR REDUCED OR ABSENCE OR MINOR
S7           0   S1(S)S2:S4
S8          20   RD S1 (unique items)
S9           2   S8/2002:2005
S10         18   S8 NOT S9
S11          2   S10 AND S2:S4
S12         16   S10 NOT S11
S13         16   Sort S12/ALL/PD,A
S14       6958   MEIOSIS OR STEROL? ?
S15    1364719   CONTAINER? ? OR CHAMBER? ? OR RECEPTACLE? ? OR CANISTER? ?
              OR VESSEL? ? OR VIAL? ? OR CAPOUL? ? OR DISH OR DISHES
S16     511346   SEAL?? OR SEALING OR ENCLOS????
S17    3907751   CLOSE OR CLOSES OR CLOSED OR CLOSING OR AIRTIGHT OR AIR()T-
             IGHT OR HERMETIC?
S18    4721727   STORE? ? OR STORING OR STORAGE OR PRESERV?
S19       9234   VITRO()(FERTILI?ATION OR MATURATION) OR IVF OR IVM
S20     182523   S5:S6(3N)S2 OR S3:S4
S21         10   S14(S)S20
S22          2   S21 AND (S15 OR S18)
S23          2   RD (unique items) [not relevant]
S24          8   S21 NOT (S22 OR S13 OR S11)
S25          8   RD (unique items)
S26          8   Sort S25/ALL/PD,A

11/3,K/1      (Item 1 from file: 98)
DIALOG(R)File  98:General Sci Abs/Full-Text
(c) 2005 The HW Wilson Co. All rts. reserv.
04045895    H.W.  WILSON  RECORD  NUMBER:  BGSI99045895    (USE FORMAT 7 FOR
FULLTEXT)
```

Sterols and isoprenoids: signaling molecules derived from the cholesterol biosynthetic pathway.

```
Edwards, Peter A
Ericsson, Johan
Annual Review of Biochemistry v. 68 (1999) p. 157-85
SPECIAL FEATURES: bibl il   ISSN: 0066-4154
 LANGUAGE:  English
COUNTRY OF PUBLICATION: United States
WORD COUNT:  13161
  (USE FORMAT 7 FOR FULLTEXT)
TEXT:
...     of farnesyl diphosphate to produce squalene (Figure 1), inhibited
the production of the superoxide ion  O2 - by human neutrophils (162).
These authors isolated presqualene diphosphate from neutrophils and
proposed that this...
...that induced meiosis when added to naked mouse oocytes (164). Recent
chemical synthesis of these  meiosis  activating  sterols  (MAS), namely
4,4-dimethyl-5a-cholesta-8, 14, 24-trien-3b-ol ("FF-MAS...
...oocyte meiosis. Interestingly, lipid extracts obtained from the testis
of breeding bulls and containing putative  meiosis - activating  sterols
were shown to activate LXRa (112). It is possible that  meiosis -
activating  sterols  stimulate meiosis by a process that is dependent upon
```

activation of LXRa.
HEDGEHOG, A PROTEIN...methylglutaryl--CoA; IPP, isopentenyl diphosphate; GPP, geranyl diphosphate; FPP, farnesyl diphosphate; GGPP, geranylgeranyl diphosphate; "MAS," **meiosis - activating sterols** ; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CE, cholesteryl esters; SR-BI, scavenger receptor...

13/3,K/2 (Item 2 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
(c) 2005 The HW Wilson Co. All rts. reserv.
03021825 H.W. WILSON RECORD NUMBER: BGSI95021825
Chemical structure of sterols that activate oocyte meiosis.
Byskov, Anne Grete
Andersen, Claus Yding; Nordholm, Lars
Nature (Nature) v. 374 (Apr. 6 '95) p. 559-62
DOCUMENT TYPE: Feature Article
SPECIAL FEATURES: bibl il ISSN: 0028-0836
LANGUAGE: English
COUNTRY OF PUBLICATION: United Kingdom
ABSTRACT: Two **meiosis - activating sterols** were isolated from human follicular fluid and bull testes, and 2 closely related C29 sterols...

13/3,K/3 (Item 3 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB
(c)2005 The Gale Group. All rts. reserv.
07796775 SUPPLIER NUMBER: 16779296 (USE FORMAT 7 OR 9 FOR FULL TEXT)
NEW DISCOVERY HOLDS OUT PROMISE OF IMPROVED TREATMENT OF INFERTILITY, AS WELL AS HORMONE-FREE CONTRACEPTION FOR WOMEN AND MEN
PR Newswire, p0406NY026
April 6, 1995
LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT
WORD COUNT: 571 LINE COUNT: 00046
... the result of collaboration between researchers at Rigshospitalet and Novo Nordisk.
The compounds (dubbed MAS: **meiosis - activating sterols**) are present in women's ovaries and in male testes. Under normal circumstances, the compounds...

13/3,K/4 (Item 4 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB
(c)2005 The Gale Group. All rts. reserv.
07788572 SUPPLIER NUMBER: 16867656
Novo Nordisk's fertility breakthrough. (meiosis activating sterols **to treat infertility)**
SCRIP World Pharmaceutical News, n2016, p28(1)
April 14, 1995
ISSN: 0143-7690 LANGUAGE: ENGLISH RECORD TYPE: CITATION

13/3,K/14 (Item 14 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)
(c) 2005 The Gale Group. All rts. reserv.
07765016 Supplier Number: 64912168 (USE FORMAT 7 FOR FULLTEXT)

meiosis - activating sterols **Novo Nordisk phase change I, Denmark, USA.**
R & D Focus Drug News, pNA
Sept 4, 2000
Language: English Record Type: Fulltext
Document Type: Magazine/Journal; Trade
Word Count: 46
(USE FORMAT 7 FOR FULLTEXT)
TEXT:
Novo Nordisk's **meiosis - activating sterol** (MAS) modulators are being evaluated in phase I trials in Denmark and the USA. These...
meiosis-activating sterols, MAS, G3G, Ovulation Stimulants, G3A, Hormonal Contraceptives, Systemic, Novo Nordisk, phase-I, Denmark, USA, new...

26/3,K/2 (Item 2 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
(c) 2005 The HW Wilson Co. All rts. reserv.
00776194 H.W. WILSON RECORD NUMBER: BGSA86026194
Methyl sterol **and cyclopropane fatty acid composition of Methylococcus capsulatus grown at** low oxygen **tensions.**
Jahnke, Linda L
Nichols, Peter D
Journal of Bacteriology (J Bacteriol) v. 167 (July 1986) p. 238-42
SPECIAL FEATURES: bibl il ISSN: 0021-9193
LANGUAGE: English
COUNTRY OF PUBLICATION: United States

```
File 155:MEDLINE(R) 1951-2005/Jul W2
         (c) format only 2005 The Dialog Corp.
Set     Items   Description
S1       4006   MEIOSIS()(ACTIVAT??? OR INDUC????)()(STEROL? ? OR SUBSTANC-
            E? ?) OR MAS
S2     266490   OXYGEN
S3       9527   CONTAINER? ? OR RECEPTACLE? ? OR VIAL? ? OR CAPOUL? ? OR (-
            SEALED OR SEALABLE)()DISH??
S4          0   S1 AND S2 AND S3
S5        150   S1 AND S2
S6         80   (MOLE OR MOLES)(2W)(LITER? ? OR LITRE? ?)
S7          0   S5 AND S6
S8    2302698   ADDITIVE? ? OR (SERUM OR RECOMBINANT)()ALBUMIN OR ENZYME? ?
             OR PHOSPHOGLYCERIDE? ? OR PROTEIN? ? OR PHOSPHOGLYCID OR PHO-
             SPHATIDYLETHANOLAMIN OR PHOSPHATIDYLCHOLINE OR PHOSPHATIDYLSE-
             RINE OR PHOSPHATIDYLNOSITOL
S9          9   S5 AND S8 [not relevant]
S10         8   S1/TI,DE AND S2/TI,DE [not relevant]
S11        88   MEIOSIS()(ACTIVAT? OR INDUC?)()(STEROL? ? OR SUBSTANCE? ?)
S12         1   S2 AND S11
S13     17612   MEIOSIS OR MEIOTIC
S14         0   S13 AND S2 AND S3
S15        89   S13 AND S2
S16        29   S8 AND S15
S17        16   S13/TI,DE AND S16
S18        16   S17 NOT (S9 OR S10 OR S12) [not relevant]
S19        53   S11/TI
S20     11409   MEIOSIS!
S21     14166   'MEIOSIS' OR R2:R7
S22    117318   STEROLS! OR DC='D10.570.938.' OR DC='D10.851.' OR DC='D4.8-
            08.247.808.'
S23        53   S21 AND S22
S24    266490   'OXYGEN' OR DC='D1.268.185.550.' OR DC='D1.362.670.'
S25         1   S23 AND S24 [a duplicate]
S26    834356   LOW
S27      2118   S26()S2
S28        13   S21:S22 AND S24 AND S27
S29         4   S8 AND S28 [not relevant]
S30         9   S28 NOT (S29 OR S25 OR S9 OR S10 OR S12 OR S18)

 12/9/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 The Dialog Corp. All rts. reserv.
13873188   PMID: 11557353
  Relation between the molecular electrostatic potential and activity of
some FF-MAS related sterol compounds.
  Boer D R; Kooijman H; van der Louw J; Groen M; Kelder J; Kroon J
  Department of Crystal & Structural Chemistry, Bijvoet Center for
Biomolecular Research, Utrecht University, Utrecht, The Netherlands.
  Bioorganic & medicinal chemistry (England)  Oct 2001,  9 (10)  p2653-9,
ISSN 0968-0896   Journal Code: 9413298
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
```

Subfile: INDEX MEDICUS

Follicular Fluid- **Meiosis Activating Sterol** (FF-MAS) is a compound important for maturation of gametes in mammals. Therefore, it may serve as a lead compound for a novel method of contraception. We studied the Molecular Electrostatic Potential of a series of active and inactive analogues of FF-MAS. We find that double bond configurations required for activity result in a local negative electrostatic potential which is larger as well as more dense compared to those of inactive molecules. We therefore hypothesize that the interaction energy of the double bond system of the MAS compounds with its receptor substantially contributes to the overall interaction energy. This notion is supported by interaction studies of the electrostatic potential originating from the double bonds in crystal structures of cholesterol and four **MAS**-derived Delta(8,14) structures synthesized and crystallized by us. In addition, we were able to derive a pharmacophore model that relates the local average ESP and its distance to the 3beta-OH **oxygen** atom to the activity of the molecules.

Tags: Female

Descriptors: *Cholestenes--chemistry--CH; *Oocytes; *Sterols--chemistry --CH; Animals; Cells, Cultured--drug effects--DE; Cholestadienols --chemistry--CH; Cholestadienols--metabolism--ME; Cholestenes--metabolism --ME; Cholesterol--chemistry--CH; Crystallography, X-Ray; Hydroxylation; Menotropins--pharmacology--PD; Mice; Models, Chemical; Molecular Conformation; Molecular Structure; Oocytes--cytology--CY; Oocytes--drug effects--DE; Oocytes--physiology--PH; Ovary--cytology--CY; Ovary--drug effects--DE; Structure-Activity Relationship

CAS Registry No.: 0 (Cholestadienols); 0 (Cholestenes); 0 (Sterols) ; 19456-83-8 (4,4-dimethylcholesta-8,14-dien-3-ol); 57-88-5 (Cholesterol); 61489-71-2 (Menotropins); 64284-64-6 (4,4-dimethylcholes ta-8,14,24-trienol)

Record Date Created: 20010914

Record Date Completed: 20011101

```
File 350:Derwent WPIX 1963-2005/UD,UM &UP=200543
         (c) 2005  Thomson Derwent
File 349:PCT FULLTEXT 1979-2005/UB=20050707,UT=20050630
         (c) 2005 WIPO/Univentio
File 348:EUROPEAN PATENTS 1978-2005/Jun W04
         (c) 2005 European Patent Office
Set      Items   Description
S1          15   AU='ANDERSEN TINA MEINERTZ' OR AU='ANDERSEN T M'
S2          29   AU='ANDERSEN T'
S3           3   AU='MULLER LARS KLINGBERG' OR AU='MULLER L K'
S4         219   AU='MULLER L'
S5           2   AU='MUELLER L K' OR AU='MUELLER LARS'
S6         238   AU='MUELLER L'
S7      147140   VITRO
S8        1840   IVF OR IVM
S9       41914   MAS OR MEIOSIS
S10          9   S1:S6 AND S7:S9
S11          3   S1:S2 AND S3:S6
S12          0   S11 NOT S10

 10/26,TI/3      (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005  Thomson Derwent. All rts. reserv.
013293517
WPI Acc No: 2000-465452/200040
  Modified release composition useful for treating inflammation and non
  insulin dependent diabetes contains
  (R)-1-(-3-(10,11-dihydro-5H-dibenzo(a,d)cyclohepten-5-ylidene)-1-propyl)-
  3-piperidinecarboxylic acid

 10/26,TI/4      (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005  Thomson Derwent. All rts. reserv.
003428477
WPI Acc No: 1982-00257J/198247
  Glycoside hydrolase inhibiting unsatd. amino-cyclitol derivs. - prepd. by
  acid-catalysed alcoholysis of oligo- or polysaccharide cpds. e.g.
  acarbose


 10/34/1      (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2005  Thomson Derwent. All rts. reserv.
014806793
WPI Acc No: 2002-627499/200267
  Closed container having low content of oxygen used for treating oocytes
  contains  meiosis  activation substance
Patent Assignee: NOVO NORDISK AS (NOVO  ); ANDERSEN T M (ANDE-I); MULLER L
  K (MULL-I)
Inventor:  ANDERSEN T M ;  MULLER L K ;  MUELLER L K
Number of Countries: 101  Number of Patents: 005
Patent Family:
Patent No      Kind   Date     Applicat No     Kind   Date      Week
WO 200262287    A1  20020815  WO 2002DK35      A   20020117  200267  B
US 20020166789  A1  20021114  US 2001273162    P   20010302  200277
                              US 200268224     A   20020205
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EP 1359881 A1 20031112 EP 2002715376 A 20020117 200377
WO 2002DK35 A 20020117
AU 2002224756 A1 20020819 AU 2002224756 A 20020117 200427
JP 2004525676 W 20040826 JP 2002562295 A 20020117 200456
WO 2002DK35 A 20020117
Priority Applications (No Type Date): DK 2001382 A 20010308; DK 2001189 A 20010206
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200262287 A1 E 23 A61J-001/00
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
US 20020166789 A1 A61K-031/00 Provisional application US 2001273162
EP 1359881 A1 E A61J-001/00 Based on patent WO 200262287
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2002224756 A1 A61J-001/00 Based on patent WO 200262287
JP 2004525676 W 35 A61J-001/00 Based on patent WO 200262287
Abstract (Basic): WO 200262287 A1

NOVELTY - Closed container having low content of an oxygen contains a **meiosis** activation substance (**MAS**) or a solid composition with high aqueous solubility containing **MAS** and an additive.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the preparation of the closed container which comprises:

(1) preparing a solid composition containing **MAS** and an additive by freeze drying and closing the container in vacuo, or

(2) preparing a solid composition containing **MAS** and an additive, filling the solid composition in a container, filling the container with an atmosphere having a low content of oxygen before, during or after filling and closing the container.

ACTIVITY - Gynecological.

MECHANISM OF ACTION - None given in the source material.

USE - Used for preparing an aqueous solution for treatment of oocytes, for in vivo fertilization and for in vivo maturation.

ADVANTAGE - The solid composition can result in germinal vehicle breakdown (GVB) of at least 50 (preferably at least 80) % when **MAS** is FF- **MAS** . The composition has good stability in water.

pp; 23 DwgNo 0/0

Technology Focus:

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: A substantial part of the atmosphere is nitrogen or argon. The content of nitrogen or argon in the atmosphere is above 90 (preferably above 95, especially above 99) v/v.%.

Preferred Composition: The container comprises oxygen (below 0.01, preferably below 0.001, especially below 0.0001 mole oxygen/l container volume or below 10, preferably below 5, especially below 1 v/v.%) in the atmosphere. The solid composition comprises organic solvent (below 10, preferably below 5, especially below 1 %), an additive (above 90, preferably above 95, especially 99 %), water or **MAS** (below 10, preferably below 5, especially below 1) wt/wt.%.

When an aqueous media is added to the solid composition, a solution

containing **MAS** is present in a concentration of 0.001 (preferably above 0.01, especially above 100) mug/ml or below 0.1 (preferably below 0.01) g/ml is obtained. When water is added to the solid composition, the content of organic solvent is present in an aqueous solution of below 0.1 (preferably 0.05, especially below 0.01) %. Preferred Process: The preparation is performed in vacuo.

BIOLOGY - Preferred Components: The additive is a protein or a phosphor glyceride (preferably serum albumin, especially human serum albumin), optionally in recombinant form

Extension Abstract:

SPECIFIC CELLS - The **MAS** comprises 4,4-dimethyl-5alpha-cholesta-8,14,24-triene-3beta-ol, 4,4-dimethyl-5alpha-cholest-8,14,24-trien-3beta-ol hemisuccinate, 5alpha-cholest-8,14-dien-3beta-ol, 5alpha-cholest-8,14-dien-3beta-ol hemisuccinate, (20S)-cholest-5-en-3beta,20-diol, 3beta-hydroxy-4,4-dimethyl-5alpha-chola-8,14-dien-24-oic acid-N-(methionine)amide, cholest-5-en-16beta-ol; or (20S)-20-((piperidin-1-yl)methyl)-4,4-dimethyl-5alpha-pregna-8,14-dien-3beta-ol.

EXAMPLE - FF-HSA (human serum albumin) was dissolved in ethanol (25 mug FF- **MAS** (**meiosis** activation substance)/ml ethanol). HSA was dissolved in water (1%). The FF- **MAS** ethanol solution (100 micro-l) and the HSA solution (350 micro-l) were mixed in a vial. The mixture was evaporated to dryness and heated at 2-8degreesC. Freshly prepared **IVM** media (500 micro-l) was added to the residue in the vial and shaken for 1-2 minutes. The **IVM** media used was TCM 199 with Earle's salt to which was added HSA (0.8%), L-glutamine (2 mM), sodium pyrovate (0.25 mm), penicillin G (100 IU/ml) and streptomycin (100 mug/ml).

The liquid was transferred to a 4-well dish and the composition was tested on oocyte obtained from immature female mice. Results showed the percentage germinal vehicle breakdown for FF- **MAS** /HAS was 97/9.

Derwent Class: B01; B04; P33; Q34
International Patent Class (Main): A61J-001/00; A61K-031/00
International Patent Class (Additional): A61J-003/00; A61K-031/575; B65D-083/04; B65D-085/42; C12M-003/00

10/34/2 (Item 2 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2005 Thomson Derwent. All rts. reserv.
013781784
WPI Acc No: 2001-265995/200127

Solid composition comprising meiosis **activating substance and an additive, useful for in-** vitro **fertilization**

Patent Assignee: NOVO NORDISK AS (NOVO)
Inventor: **ANDERSEN T M**
Number of Countries: 095 Number of Patents: 013
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200119354	A2	20010322	WO 2000DK500	A	20000911	200127	B
AU 200069850	A	20010417	AU 200069850	A	20000911	200140	
NO 200201309	A	20020315	WO 2000DK500	A	20000911	200241	
			NO 20021309	A	20020315		
EP 1216059	A2	20020626	EP 2000958274	A	20000911	200249	
			WO 2000DK500	A	20000911		
CZ 200200591	A3	20020814	WO 2000DK500	A	20000911	200263	

			CZ 2002591	A	20000911		
KR 2002032593	A	20020503	KR 2002703526	A	20020316	200270	
ZA 200201383	A	20021127	ZA 20021383	A	20020219	200305	
HU 200202630	A2	20021228	WO 2000DK500	A	20000911	200308	
			HU 20022630	A	20000911		
CN 1373675	A	20021009	CN 2000812882	A	20000911	200309	
JP 2003509365	W	20030311	WO 2000DK500	A	20000911	200319	
			JP 2001522989	A	20000911		
MX 2002002439	A1	20020801	WO 2000DK500	A	20000911	200367	
			MX 20022439	A	20020306		
BR 200014058	A	20040330	BR 200014058	A	20000911	200424	
			WO 2000DK500	A	20000911		
US 6844313	B1	20050118	US 2000661696	A	20000914	200506	

Priority Applications (No Type Date): DK 991308 A 19990916

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200119354	A2	E	11	A61K-031/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200069850	A		A61K-031/00	Based on patent WO 200119354
NO 200201309	A		A61K-000/00	
EP 1216059	A2	E	A61K-047/42	Based on patent WO 200119354

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CZ 200200591	A3		A61K-047/42	Based on patent WO 200119354
KR 2002032593	A		A61K-031/00	
ZA 200201383	A	23	A61K-000/00	
HU 200202630	A2		A61K-047/42	Based on patent WO 200119354
CN 1373675	A		A61K-047/42	
JP 2003509365	W	17	A61K-045/00	Based on patent WO 200119354
MX 2002002439	A1		A61K-031/00	Based on patent WO 200119354
BR 200014058	A		A61K-031/00	Based on patent WO 200119354
US 6844313	B1		A01N-037/18	

Abstract (Basic): WO 200119354 A2

NOVELTY - A solid composition comprising **meiosis** activating substance (**MAS**) and an additive has good solubility in water, and is used for preparing an aqueous solution for treating oocytes.

DETAILED DESCRIPTION - A solid composition comprising **MAS** and an additive; an aqueous solution comprising **MAS** ; and a device having a hollow containing the solid product or solution, are new.

USE - The solid composition is used to prepare an aqueous solution for treatment of oocytes, resulting in a percentage germinal vesicle breakdown (GVB) of at least 50% (preferably at least 80%) when **MAS** is FF- **MAS** . The oocytes become more prone to becoming fertilized.

pp; 11 DwgNo 0/0

Technology Focus:

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: A solid composition contains less than 50% (preferably less than 5%) **MAS** ; less than 10% (preferably less than 1%) water, and less than 10% (preferably less than 1%) organic solvent. An aqueous solution comprises at least 0.001 (preferably at least 0.5) microg/ml **MAS** .

Preferred Compounds: The **MAS** is

4,4-dimethyl-5alpha-cholesta-8,14,24 triene-3beta-ol (FF- **MAS**) or its hemisuccinate; 5alpha-cholest-8,14dien 3beta-ol or its hemisuccinate; (20S)-cholest-5-en-3beta,20-diol; 3beta hydroxy-4,4-dimethyl-5alpha-chola-8,14-dien-24-oic acid-N (methionine)amide; and cholest-5-en-16beta-ol. The additive is a protein or a phosphoglyceride.

Extension Abstract:

EXAMPLE - Solutions of 4,4-dimethyl-5alpha-cholesta-8,14,24 triene-3beta-ol (FF- **MAS**) in water/ethanol containing human serum albumin (HSA) were evaporated to dryness. Before use, MEM ALPHA medium (500 microl) was added, and within 30 minutes at room temperature, a clear solution of FF- **MAS** and HSA was obtained. The formulations were tested on oocytes obtained from immature female mice, and a formulation comprising FF- **MAS** solution in ethanol (26.1 microg/ml, 100 microl) and 20% HSA solution in water (250 microl), having ratio FF- **MAS** :HSA 1:2000, had 93% germinal vesicle breakdown.

Derwent Class: B01
International Patent Class (Main): A01N-037/18; A61K-000/00; A61K-031/00; A61K-045/00; A61K-047/42
International Patent Class (Additional): A61K-031/565; A61K-031/569; A61K-031/575; A61K-047/22; A61P-015/00; C12M-001/00; C12N-005/00

10/3,AB,IC/7 (Item 3 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2005 WIPO/Univentio. All rts. reserv.
00573708
NOVEL FORMULATION
NOUVELLE FORMULATION
Patent Applicant/Assignee:
NOVO NORDISK A S,
Inventor(s):
ANDERSEN Tina Meinertz ,
HJORTH Thyge Borup,
JORGENSEN Kim Westi
Patent and Priority Information (Country, Number, Date):
Patent: WO 200037081 A1 20000629 (WO 0037081)
Application: WO 99DK699 19991214 (PCT/WO DK9900699)
Priority Application: DK 981703 19981222
Designated States:
(Protection type is "patent" unless otherwise stated - for applications prior to 2004)
AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
Main International Patent Class: A61K-031/445
International Patent Class: A61K-009/22; A61K-047/38
Publication Language: English
Fulltext Word Count: 5009
English Abstract

A modified release formulation contains (R)-1-(3-(10,11- Dihydro-5H-dibenzo [a,d]cyclo -hepten-5- ylidene) -1-propyl) -3-piperidinecarboxylic acid or pharmaceutically compound thereof.

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File 155:MEDLINE(R) 1951-2005/Jul W2
         (c) format only 2005 The Dialog Corp.
File   5:Biosis Previews(R) 1969-2005/Jul W1
         (c) 2005 BIOSIS
File  73:EMBASE 1974-2005/Jul 08
         (c) 2005 Elsevier Science B.V.
File  34:SciSearch(R) Cited Ref Sci 1990-2005/Jul W1
         (c) 2005 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File  71:ELSEVIER BIOBASE 1994-2005/Jul W1
         (c) 2005  Elsevier Science B.V.
File 357:Derwent Biotech Res. _1982-2005/Jul W2
         (c) 2005 Thomson Derwent & ISI
File 358:Current BioTech Abs 1983-2005/Jun
          (c) 2005 DECHEMA
File 285:BioBusiness(R) 1985-1998/Aug W1
         (c) 1998 BIOSIS
Set     Items   Description
S1       2324   AU=(ANDERSEN T? OR ANDERSEN, T?)
S2       4132   AU=(MULLER L? OR MULLER, L? OR MUELLER L? OR MUELLER, L?)
S3     130273   MEIOSIS OR MEIOTIC OR MAS
S4      69902   IVF OR IVM OR VITRO()(FERTILI?ATION OR MATURATION)
S5         11   S1:S2 AND S3:S4
S6          9   RD (unique items)
S7          9   Sort S6/ALL/PY,A

 7/6/1      (Item 1 from file: 155)
07845432   PMID: 3105097
   [Ovulation induction for in vitro fertilisation at the Tygerberg Hospital]
  Ovulasie-induksie vir in vitro-bevrugting in Tygerberg-hospitaal.
Apr 18 1987

 7/6/3      (Item 3 from file: 5)
0008649962   BIOSIS NO.: 199345080944
Vitamin D3 improves subnormal in  vitro  maturation  in monocytes from
  AIDS-patients
BOOK TITLE: IXth International Conference on AIDS in affiliation with the
  IVth STD World Congress
1993

 7/6/4      (Item 4 from file: 34)
06093979   Genuine Article#: XU741   Number of References: 83
Title: Theory and practice of immunocontraception in wild mammals  (
    ABSTRACT AVAILABLE)
Publication date: 19970600

 7/6/5      (Item 5 from file: 71)
01538073        2000217625
Inhibition of cyclin-dependent kinase 4 (Cdk4) by fascaplysin, a marine
  natural product
PUBLICATION DATE: September 7, 2000

 7/6/6      (Item 6 from file: 71)
01477267        2000149527
Novel Cdk inhibitors restore TGF-beta sensitivity in Cdk4 overexpressing
```

epithelial cells
PUBLICATION DATE: June 16, 2000

7/6/7 (Item 7 from file: 71)
01720616 2001083155
Selective in vivo and in vitro effects of a small molecule inhibitor of cyclin-dependent kinase 4
PUBLICATION DATE: March 21, 2001

7/6/8 (Item 8 from file: 34)
11079991 Genuine Article#: 602CE Number of References: 86
Title: Determination of multiple torsion-angle constraints in U-C-13,N-15-labeled peptides: 3D H-1-N-15-C-13-H-1 dipolar chemical shift NMR spectroscopy in rotating solids (ABSTRACT AVAILABLE)
Publication date: 20021009

7/6/9 (Item 9 from file: 155)
14418574 PMID: 12355536
PX4+, P2X5+, and P5X2+ (X=Br, I) salts of the superweak Al(OR)4- anion [R=C(CF3)3].
Oct 4 2002